

CLAIMS

1. An optionally modified oligonucleotide comprising from 8 to 50 nucleotides which hybridizes specifically to the sequence SEQ ID No. 1 and which inhibits OB-RGRP expression.
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2. The oligonucleotide as claimed in claim 1, which promotes the expression of leptin receptors at the cell surface.
- 10 3. The oligonucleotide as claimed in either of claims 1 and 2, which is an antisense oligonucleotide.
- 15 4. The oligonucleotide as claimed in one of claims 1 to 3, which comprises a sequence exhibiting at least 60% identity with the sequence SEQ ID No. 2.
5. The oligonucleotide as claimed in one of claims 1 to 3, wherein nucleotides are thioesterified.
- 20 6. The oligonucleotide as claimed in one of claims 1 to 3, wherein nucleotides are 2'-O-methylated.
7. The oligonucleotide as claimed in one of claims 1 to 3, which has a triethylene glycol residue at its 3' end.
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8. The oligonucleotide as claimed in one of claims 1 to 3, which is single-stranded.
9. The oligonucleotide as claimed in one of claims 1 to 8, which 30 comprises a sequence exhibiting at least 60% identity with the sequence SEQ ID No. 2, in which the nucleotides at positions 2, 4, 6, 7, 9, 11, 13, 15, 17, 19 and 20, in the 5' to 3' direction, are thioesterified.
- 35 10. The oligonucleotide as claimed in one of claims 1 to 8, which comprises a sequence exhibiting at least 60% identity with the sequence SEQ ID No. 2, in which the nucleotides at positions 1, 2, 3, 4, 5, 16, 17, 18, 19 and 20, in the 5' to 3' direction, are 2'-O-methylated.

11. The oligonucleotide as claimed in one of claims 1 to 10, which is a DNA.
- 5 12. An oligonucleotide of the iRNA type comprising from 10 to 60 nucleotides, which hybridizes specifically to the sequence SEQ ID No. 21 and which inhibits the expression of OB-RGRP.
- 10 13. The oligonucleotide as claimed in claim 12, which is a double-stranded RNA.
14. A vector expressing an oligonucleotide as claimed in one of claims 1 to 4 and 12.
- 15 15. A cell containing a vector as claimed in either of claims 13 and 14.
16. A medicinal product containing an oligonucleotide, a vector or a cell as claimed in one of claims 1 to 15.
- 20 17. A pharmaceutical composition containing a pharmacologically active amount of an oligonucleotide, of a vector or of a cell as claimed in one of claims 1 to 15 and pharmaceutically acceptable excipients.
- 25 18. The use of an oligonucleotide, of a vector or a cell as claimed in one of claims 1 to 15, for producing a medicinal product for preventing and/or treating leptin-related pathological conditions.
- 30 19. A fusion protein, which is composed of a sequence exhibiting at least 65% identity with the sequence SEQ ID No. 4, or the sequence SEQ ID No. 16, or of a substantial part of the sequence SEQ ID No. 4 or of the sequence SEQ ID No. 16, and of an energy-donor or energy-acceptor protein, or of a substantial and active part of an energy-donor or energy-acceptor protein.
- 35 20. The fusion protein as claimed in claim 19, wherein the protein is a luciferase.
21. The fusion protein as claimed in claim 19, wherein the protein is GFP or a mutant of this protein or DsRed.

22. The fusion protein as claimed in claim 19, wherein the mutant of GFP is YFP, EYFP, wild-type GFP, GFPS65T or Topaz.

5 23. The fusion protein as claimed in claim 19, which has the sequence SEQ ID No. 6, SEQ ID No. 8, SEQ ID No. 18 or SEQ ID No. 20.

24. A nucleic acid encoding one of the proteins as claimed in one of claims 19 to 23.

10 25. The nucleic acid as claimed in claim 24, which has the sequence SEQ ID No. 5, SEQ ID No. 7, SEQ ID No. 17 or SEQ ID No. 19.

15 26. A nucleic acid which exhibits at least 65% identity with the sequence as claimed in claim 25.

27. A nucleic acid which hybridizes, under high stringency conditions, with the sequence as claimed in claim 25.

20 28. A cell comprising a nucleic acid as claimed in one of claims 24 to 27.

29. A cell expressing a protein as claimed in one of claims 19 to 23.

30. A fragment of a cell as claimed in either of claims 28 and 29.

25 31. A lysate of a cell as claimed in either of claims 28 and 29.

32. A membrane of a cell as claimed in either of claims 28 and 29.

30 33. A method for determining the modification, by a compound, of the interaction between a protein exhibiting at least 65% identity with the sequence SEQ ID No. 4 or the sequence SEQ ID No. 16, and the leptin receptor, comprising the steps consisting in:
- bringing said compound into contact with a protein exhibiting at least 65% identity with the sequence SEQ ID No. 4 or the sequence SEQ ID No. 16, and the leptin receptor, or cells, or fragments or lysates or membranes of cells, comprising such proteins, and optionally a suitable enzyme substrate, and

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- measuring the interaction between the protein exhibiting at least 65% identity with the sequence SEQ ID No. 4 or the sequence SEQ ID No. 16, and the leptin receptor.

5 34. A method for determining the modification, by a compound, of the interaction between a protein exhibiting at least 65% identity with the sequence SEQ ID No. 4 or the sequence SEQ ID No. 16, and the leptin receptor, comprising the steps consisting in:

- bringing said compound into contact with an energy-donor fusion protein and an energy-acceptor fusion protein, or cells, or fragments or lysates or membranes of cells, comprising such a protein, and optionally a suitable enzyme substrate, and
- measuring the energy transfer.

10 35. The method as claimed in claim 34, wherein the energy-donor fusion protein is a protein from fusion between the leptin receptor, or a substantial part of the leptin receptor, and luciferase, or a substantial part of luciferase, and the energy-acceptor fusion protein is a fusion protein as claimed in claim 22.

15 36. The method as claimed in claim 34, wherein the energy-donor fusion protein is a fusion protein as claimed in claim 20, and the energy-acceptor fusion protein is a protein from fusion between the leptin receptor, or a substantial part of the leptin receptor, and YFP, or a substantial part of YFP.

20 37. The method as claimed in claim 34, wherein the energy transfer measured in the presence of the test compound is compared to that measured in the absence of the test compound.

25 38. The method as claimed in claim 34, wherein the energy transfer measured in the presence of the test compound and the leptin (or a ligand of the receptor) is compared to that measured in the presence of the compound in the absence of leptin (or a ligand of the receptor).

30 39. A method for screening or detecting compounds intended for the prevention and/or treatment of leptin-related pathological conditions, comprising the steps consisting in:

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- bringing said compound into contact with a protein exhibiting at least 65% identity with the sequence SEQ ID No. 4 or the sequence SEQ ID No. 16, and the leptin receptor, or cells, or fragments or lysates or membranes of cells, comprising such proteins, and 5 optionally a suitable enzyme substrate, and
 - measuring the interaction between a protein exhibiting at least 65% identity with the sequence SEQ ID No. 4 or the sequence SEQ ID No. 16, and the leptin receptor.

10 40. The method as claimed in either of claims 34 and 35, wherein the fusion protein is a protein of sequence SEQ ID No. 6, SEQ ID No. 8, SEQ ID No. 12, SEQ ID No. 14, SEQ ID No. 18 or SEQ ID No. 20.

15 41. The method as claimed in one of claims 33 to 40, wherein the cells are treated with a permeabilizing agent.

20 42. The oligonucleotide as claimed in claim 12, which is a double-stranded iRNA in which at least one of the two strands comprises a sequence exhibiting at least 60% identity with one of the sequences SEQ ID No. 37 or SEQ ID No. 38.

43. The oligonucleotide as claimed in claim 12, which is a single-stranded iRNA and comprises a sequence exhibiting at least 60% identity with the sequence SEQ ID No. 42.

25 44. The oligonucleotide as claimed in claim 43, wherein the iRNA comprises a loop.